REMARKS

Applicant wishes to express appreciation for the courtesies extended to Applicant's representative, Lars Genieser, by Examiner Ardin Marschel during a telephonic interview on August 3, 2009.

Reconsideration is respectfully requested in light of the amendments above and the remarks that follow.

Claims 1-2, 9-10, and 17-18 are pending. Claims 3-6 and 11-14 are withdrawn. Claims 7-8 and 15-16 have been canceled. Claims 1, 9-10, and 13-14 have been amended. Support for amended claims 1, 9-10, and 13-14 is found, for example, in paragraphs [00012], [00076]-[00077] of the specification as filed.

Claims 1-2, 9-10, and 15-18 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,656,651 to Sovak et al. (herein, "Sovak"), in view of U.S. Patent No. 6,949,521 to Chu et al. (herein, "Chu"). Applicant respectfully traverses.

Claims 15-16 have been canceled, rendering their rejection moot.

Claims 1, 9, and 10 have been amended to pertain to compounds of which the substituent R is $N_3C_6H_4$ (azidophenyl). Sovak does not present an example of a compound in which a phenyl group is directly attached to the nitrogen at the R position of the structure shown in column 3 of Sovak. Any examples in Sovak having an aromatic constituent of the R group are instead attached to the nitrogen through a non-aromatic constituent.

One of ordinary skill in the art would not have expected results obtained with a compound having a non-aromatic constituent attached to the nitrogen at the R position to have any predictive value for the case of a phenyl attached at the R position. The unpredictable effect of even small changes in structure on the pharmaceutical activity of a compound is discussed in the attached Declaration of Michael E. Jung, Ph.D. Thus, one of ordinary skill in the art would have had no reasonable expectation of success in obtaining a pharmaceutically active compound by modifying a compound of Sovak having a non-aromatic group at the R position to have a phenyl ring at that position. Rather, as indicated in the attached Declaration, that the 4-[3-(azidophenyl)-4,4-dimethyl-5-oxo-2-thioxoimidazolidin-1-yl]-2-trifluoromethylbenzonitrile

compound of claim 1 exhibited strong antagonistic effects on the ligand binding domain of the androgen receptor, did not exhibit agonistic effects, and inhibited the growth of the LNCaP hormone-refractory prostate cancer cell line was surprising and unexpected.

The Federal Circuit recently reiterated that "an obviousness argument based on structural similarity between claimed and prior art compounds 'clearly depends on a preliminary finding that one of ordinary skill in the art would have selected [the prior art compound] as a lead compound." *See*, *Procter & Gamble Co. v. Teva Pharmaceuticals USA*, Inc. (Fed. Cir., May 13, 2009), *quoting Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1359 (Fed. Cir. 2007). As the Examiner states on page 6 of the Office Action, Sovak indicates that the R group "may be aliphatic, alicyclic, aromatic, heterocyclic, or combinations thereof." There is no guidance provided as to which of this plethora of potential functional groups should be selected for a lead compound. Moreover, in *Procter & Gamble*, the Federal Circuit went on to require that "it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound". *See*, *Procter & Gamble*, *quoting Takeda*, 492 F.3d at 1356-57. As discussed above, given the unpredictability of the pharmaceutical art and of the anti-cancer chemotherapeutic field, the Examiner identifies no reason that would have led one of ordinary skill in the art to modify any of the compounds presented in Sovak to yield a compound such as that of claim 1, in which the R substituent is a phenyl group.

Furthermore, as the Examiner concedes on page 7 of the Office Action, Sovak does not teach the 4-[3-(azidophenyl)-4,4-dimethyl-5-oxo-2-thioxoimidazolidin-1-yl]-2-trifluoromethylbenzonitrile compound of claim 1, in which the N substitution at the R position is $C_6H_4N_3$. The Examiner suggests that Chu teaches azide derivatives of drugs and can be combined with Sovak to yield the compound of claim 1. Applicant maintains that this is not the case. As discussed in the attached Declaration, there are strong disincentives that lead one of ordinary skill in the art away from modifying a pharmaceutical compound with an azide substituent. These disincentives include photoreactivity of the azide group, with consequent instability of the azide-derivatized compound, and undesired reaction of the azide group with reducing agents in cells. That is, contrary to the Examiner's suggestion, one of ordinary skill would not conclude from Chu that the derivatization of a drug with an azide functionality offers

a general route to extending the half-life of such a drug. Moreover, one of ordinary skill in the art would appreciate that the derivatization of a drug with an azide functionality could have detrimental effects on characteristics of the drug, such as shelf life. Therefore, one of ordinary skill in the art aware of Sovak and Chu would not have been motivated to modify a compound of Sovak by functionalizing it with an azide group.

On page 2 of the preceding Office Action dated July 23, 2008, Examiner Rao indicated that several citations on the forms PTO/SB/08A/B submitted November 1, 2007 and August 24, 2006 were lined out and not considered. Applicant's representative discussed these non-considered references with Examiner Ardin Marschel on August 3, 2009. Examiner Marschel indicated that several of the references should be considered by the USPTO, for the following reasons:

- Examiner Marschel indicated that although the documents of citations B2 (international application publication WO 00/17163) and B3 (international application publication WO 90/13646) on page 2 of the form PTO/SB/08A/B submitted November 1, 2007 were not in entirely in English, because an English abstract and chemical structures and biotechnological diagrams and symbols in an internationally recognized format were included with each document, the cited documents should be considered by the USPTO.
- Examiner Marschel indicated that International Search Reports (ISRs) are to be considered by the USPTO under current practice, even though ISRs do not include a publication date. Therefore, the ISRs of citation CA on the form PTO/SB/08A/B submitted August 24, 2006 and of citations C85 and C86 on the form PTO/SB/08A/B submitted November 1, 2007 should be considered by the USPTO.
- Applicant herewith provides the publication dates of the non-patent literature documents of citations C3 and C9 on page 2 of the form PTO/SB/08A/B submitted November 1, 2007, and, therefore, submits that these non-patent literature documents should now be considered:

  [C3]: Karp et al., Cancer Res. 56 (Dec. 15, 1996) 5547-5556.

  [C9]: Graham and van der Eb, Virology, 52(2) (April 1973) 456-467.

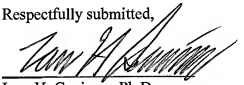
For these reasons, Applicant respectfully requests that the Examiner consider all of the citations previously submitted in Information Disclosure Statements, including citations CA of form PTO/SB/08A/B submitted August 24, 2006 and citations B2, B3, C3, C9, C85, and C86 of form PTO/SB/08A/B submitted November 1, 2007, and provide applicant with the corresponding forms PTO/SB/08A/B, signed and dated by the Examiner to indicate the date the citations were considered.

For the reasons provided above, claims 1, 9, and 10 have not been shown to be *prima facie* obvious over the combination of Sovak and Chu. As such, at least claims 1, 9, and 10, and claims 2, 17, and 18 dependent therefrom are patentable, and Applicant respectfully requests that the rejection of claims 1-2, 9-10, and 17-18 be withdrawn.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is hereby invited to telephone the undersigned at the number provided.

Applicants respectfully request that a Notice of Allowance of all pending claims not withdrawn, at least claims 1-2, 9-10, and 17-18, be timely issued in this case.

Respectfully submitted,



Date: August 27, 2009

Lars H. Genieser, Ph.D.
Registration No. 46,722
VENABLE LLP
P.O. Box 34385
Washington, D.C. 20043-9998
Telephone (Direct): (202) 344-8234
Telephone (Main): (202) 344-4000
Telefax: (202) 344-8300

DC2/1049576